EXHIBIT A

Skull Base, Anatomy

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Synonyms and related keywords: anterior cranial fossa, middle cranial fossa, posterior cranial fossa, skull base, head anatomy, skull anatomy

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Disclosure

The complexity of the human form perhaps reaches its apogee in the myriad of intricate structures that course through and are encased within the skull. The knowledge of normal anatomy and common variations is essential for the treatment of pathology and surgical manipulation in and around the skull base.

The 5 bones that make up the skull base are the ethmoid, sphenoid, occipital, paired frontal, and paired parietal bones. The skull base can be subdivided into 3 regions, as follows: the anterior, middle, and posterior cranial fossa. This article discusses each region separately with attention to surrounding structures, nerves, vascular supply, and landmarks.

Boundaries

The anterior limit of the anterior skull base is the posterior wall of the frontal sinus, which is formed from the frontal bone. The falx cerebri inserts posteriorly along the midline frontal crest. The posterior limit is the lesser wing of the sphenoid and planum sphenoidale. The lateral boundaries are formed by the frontal bone.

The greater anterior portion of the floor is convex and grooved by the frontal lobe gyri; this segment is

made up of the orbital portion of the frontal bone. The central part of the floor is formed by the ethmoid bone and is the deepest portion. The center of this portion is the cribriform plate and fovea ethmoidalis, which forms the roof of the ethmoid sinus. The foramen cecum sits between the frontal crest and the prominent crista galli, which projects up centrally between the hemispheres. Lateral to this projection, numerous small foramina within the cribriform plate transmit olfactory nerves from the nasal mucosa to the olfactory bulb. The posterior limit of the floor is formed by the sphenoid bone and the central planum sphenoidale, an important landmark in anterior fossa surgery.

The optic chiasm or chiasmatic sulcus sits midline and just to the posterior. The posterolateral segment is formed by the lesser wing of the sphenoid. This forms the roof of the optic canal and is a sharp definite boundary, related to the lateral cerebral sulcus and sphenoparietal sinus. Medially, the lesser wing of the sphenoid forms the anterior clinoid process, an important landmark for the optic nerve and supracavernous internal carotid artery (see Image 1).

Inferior relationships

The most important anatomical structures below the anterior cranial fossa are the orbits and the paranasal sinuses. A thorough description is beyond the scope of this article, but some important anatomy and relationships are discussed.

The bony orbit is often a route for intracranial and extracranial spread of infection and tumors due to its direct proximity to the anterior fossa. The posterior wall is thin and is adjacent to the superior sagittal sinus and frontal lobe dura. The posterior aspect includes the optic canal, the superior orbital fissure (SOF), and the inferior orbital fissure (IOF). The SOF conveys the oculomotor (III), trochlear (IV), abducens (VI), and ophthalmic nerves (V1), and ophthalmic veins. The IOF transmits the maxillary nerve (V2) and the infraorbital vessels, and communicates with the infratemporal and pterygomaxillary fossae. Lastly, the optic canal transmits the optic nerve (II) and ophthalmic artery.

Image 2 demonstrates the relationship of these openings. The medial wall is closest to the apex and is formed by the orbital process of the frontal, lacrimal, ethmoid, and sphenoid bones. The lesser wings of the sphenoid and the frontal process of the maxilla form the lateral walls. The posterior-most segment of the lateral orbital wall forms the anterior wall of the middle cranial fossa and will be discussed in greater detail in the next section.

The ethmoid sinuses are housed inferior to the anterior fossa and medial to the orbits. The frontal sinus can be a point of entry into the anterior fossa, due to trauma, tumor, infection, or surgery. It is made from the frontal bone and has a thick anterior and thinner posterior wall, which relates to the superior sagittal sinus and the frontal lobe dura.

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The dura mater attaches anteriorly at the frontal crest and crista galli to form the falx cerebri, a ligamentous sheath that carries the superior and inferior sagittal sinuses. The superior sagittal sinus drains the superior cerebral and frontal diploic veins of Breschet. The foramen cecum is usually blind but will occasionally contain a vein from the nasal mucosa to the superior sagittal sinus.

The frontal lobes occupy the anterior fossa and sit superior to the orbits and sinonasal tract. The major structures in this area are the olfactory bulb and tract. The olfactory bulb lies along the medial edge of the frontal orbital plate and connects with the olfactory tract, which courses above the cribriform plate and planum sphenoidale.

Boundaries

The greater wing of the sphenoid forms the anterior wall of the middle skull base. The posterior limit is the clivus and, laterally, the posterior surface of the petrous bone. The lateral wall is made up from the greater wing of the sphenoid anteriorly and the squamous portion of the temporal bone posteriorly.

The body of the sphenoid makes up the central portion of the middle fossa. The tuberculum sellae sits on the anterior slope between the chiasmal sulcus and the sella turcica. Just posterior to the tuberculum sellae lies the dorsum sellae and, superiorly and laterally, the posterior clinoid processes. The anterior and posterior clinoid processes are important landmarks and areas of dural attachment. The sides of the body of the sphenoid slope laterally and inferiorly to meet the floor and form the middle cranial fossa proper. In this region lies the sigmoid groove for the internal carotid artery as it traverses the petrous apex through the cavernous sinus.

The floor is made of the greater wing of the sphenoid anteriorly, followed by the squamous portion of the temporal bone and the petrous ridge of the temporal bone posteriorly. The floor and the lateral walls are grooved for the middle meningeal artery, which courses anterolaterally from the foramen spinosum and divides into the frontal and parietal branches; the former ascends across to the pterion, where it courses backward. The pterion is an H-shaped suture where the frontal bone, greater wing of the sphenoid bone, squamous temporal bone, and parietal bone meet. It is approximately 3.5 cm behind the zygomaticofrontal suture and 4 cm above the zygomatic arch. The pterion marks the axial extent of the lesser wing of the sphenoid.

The petrous ridge has many important areas and is longitudinally grooved by the superior petrosal sinus. The medial surface is home to the trigeminal ganglion in the Meckel cave, which is near the apex. The internal carotid artery runs inferior to this area, and, frequently, its bony canal may be dehiscent, making dural elevation risky. Anteromedially, just lateral to the arcuate eminence, lie the canals for the greater and lesser superficial petrosal nerves (LSPNs); these structures are important landmarks for middle cranial fossa approaches to the internal auditory canal (IAC). The arcuate eminence is the superior extent of the superior semicircular canal; laterally, the middle ear and mastoid are covered by the thin tegmen tympani. The tegmen tympani is a thin plate of bone that separates the middle lobe dura from the middle ear cavity. The bone of the middle fossa floor may be dehiscent over the geniculate ganglion.

Foramina

From anterior to posterior lie the SOF, foramen rotundum, foramen ovale, and foramen spinosum. The SOF extends inferomedially and toward the orbital apex and transmits the oculomotor (III); trochlear (IV); lacrimal, frontal, and nasociliary branches of V1; and abducens (VI) nerves; and the superior ophthalmic vein. The foramen rotundum lies posteroinferiorly and transmits the maxillary division (V2) of the trigeminal nerve into the pterygopalatine fossa. The foramen sits near the lateral wall of the sphenoid sinus. The foramen ovale is posterior and lateral and transmits the mandibular division (V3) of the trigeminal nerve, the accessory meningeal artery, the LSPN, and emissary veins to the pterygoid plexus and infratemporal fossa. Further posteriorly and laterally lies the small foramen spinosum, which shuttles the middle meningeal artery and the meningeal branch of the facial nerve (VII) (see Image 3).

The carotid canal is formed where the petrous apex articulates with the sphenoid and occipital bone medially, and is continued by the foramen lacerum on the undersurface of the skull base. The foramen lacerum is posterior and medial to the foramen ovale. Further posteriorly, the trigeminal ganglion sits in a depression on the anterior surface of the petrous temporal bone in the Meckel cave. Two inconsistent foramina are the innominate, which may be found medial to the foramen spinosum, and the foramen of Vesalius, found medial to foramen ovale. The foramen of Vesalius is found in 40% of individuals and transmits an emissary vein from the cavernous sinus.

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The dura is strongly adherent to the clinoid processes, petrous and sphenoid ridges, and the basal foramina. In the midline, it forms the diaphragma sellae, which covers the pituitary fossa and is perforated by the pituitary stalk. The cavernous sinus resides on both sides of the body of the sphenoid bone. The temporal lobe takes up most of the space of the middle fossa and extends to the inferior portion of the anterior fossa. The greater superficial petrosal nerve (GSPN) and rostral LSPN run along the floor beneath the dura and parallel the anterior edge of the petrous bone into foramen lacerum. Here, the GSPN forms the nerve of the pterygoid canal with the deep petrosal nerve. This area is a landmark for the inner carotid artery (ICA), which lies deep and parallel to the temporal bone and medial to the styloid process.

The facial (VII) and vestibulocochlear (VIII) nerves originate from the caudal pons, course through the subarachnoid space, and enter the porus acusticus and IAC. Cranial nerve VII continues through the middle ear to the mastoid. The eustachian tube originates at the protympanum and runs anteromedially and inferiorly. The bone directly medial to the eustachian tube may be dehiscent and the ICA may be seen, which is clinically relevant during surgical middle fossa exploration, as the eustachian tube must be traversed before reaching the ICA in this area.

Cavernous sinus

The cavernous sinus is a complex plexus of veins within the dura that sits beside the sphenoid sinus and extends from the SOF to the apex of the petrous temporal bone. The anterior and posterior petroclinoid folds serve as the lateral borders. Along the lateral wall runs the ICA, giving off 2-6 caroticocavernous branches that supply the hypophysis and join branches from the middle meningeal artery. Running lateral to the ICA, the abducens (VI) nerve enters the dura superior to the clivus and

enters the Dorello canal. The petroclinoid and petrosphenoidal ligaments of Gruber form the roof of the canal and it lies in close proximity to the trigeminal ganglion and within 3 mm of the sphenoid sinus.

Running posteroanteriorly within the lateral wall are the oculomotor (III), trochlear (IV), ophthalmic (V1), and maxillary (V2) nerves. The oculomotor nerve divides into superior and inferior divisions at the most anterior portion of the cavernous sinus. The trochlear nerve enters at the angle between the anterior and posterior petroclinoid folds and courses the lateral wall. The 3 divisions of the trigeminal traverse inferior to the tentorium cerebelli into the Meckel cave, within the subarachnoid space. This cave is home to the trigeminal or Gasserian ganglion overlying the petrous apex and ICA. From here, V1, V2, and V3 pass into the lateral wall of the cavernous sinus.

An understanding of the complex network of venous drainage is crucial to performing middle fossa surgery. The cavernous sinus connects anteriorly to the superior ophthalmic vein and the sphenoparietal sinus and drains posteriorly into the superior and inferior petrosal sinuses, en route to the basilar plexus. Medially it forms the circular sinus via connections to anterior and posterior intercavernous plexuses. The superficial, middle, and inferior cerebral veins drain into the cavernous sinus from above, and the emissary veins drain into the pterygoid plexus below the sinus. An interruption of the anastomotic branch of the superficial middle cerebral vein as it connects to the transverse sinus is likely to cause an infarction.

Rarely, infections may enter the skull base from the facial venous system and travel retrograde through the valveless ophthalmic veins into the anterior portion of the cavernous sinus, resulting in cavernous sinus thrombosis. Pimples and pustules of the face may seed infection through the angular vein, while dental infections may spread via the pterygoid plexus.

Internal carotid artery

The course of the ICA is complex, and landmarks need to be recognized during skull base surgery. The course can be divided into 4 parts: cervical, intratemporal, cavernous, and supracavernous (see Image 5).

The cervical portion passes near the third and fourth cervical vertebrae. At this point, it is deep to the posterior digastric muscle and styloid process and superior and posteromedial to the external carotid artery. The cervical ICA can be distinguished from the external carotid because it has no branches; this is important clinically as the relationship with the external carotid may be aberrant. The ICA enters the petrous bone via the carotid foramen and runs cranially into foramen lacerum.

The intratemporal segment is difficult to mobilize because of an adherent fibrous ring. This vertical portion ascends 5 mm and turns anteromedially into the horizontal portion. At this point, it is medial to the eustachian tube and anterolateral and just below the cochlea. It now runs forward along the petrous bone at an angle of 45° to the midsagittal plane, giving off the caroticotympanic and pterygoid branches. At this point, the artery is superior and lateral to the sphenoid bone, in an area referred to as the carotid siphon. The artery then enters the cavernous sinus medial to the abducens nerve (VI).

Upon traversing the roof of the cavernous sinus medial to the anterior clinoid process, the ICA now enters the supracavernous portion. The last segment turns backward under the optic nerve to the anterior perforated substance where it joins the circle of Willis via its terminal anterior and middle cerebral arteries.

Inferior relationships

Lateral structures

The infratemporal fossa lies below the temporal bone, inferomedial to the zygomatic arch, posterior to the maxilla, and serves as an access point to the nasopharynx. Many important structures lie in this region. The deep lobe of the parotid gland and the accompanying facial (VII) nerve and its branches may be found here (see Image 6). Important contents include the pterygoid venous plexus, internal maxillary artery, V2, and the chorda tympani branch of the facial nerve, which supplies taste sensation to the anterior two thirds of the tongue. Access to the infratemporal fossa proper can be obtained by reflecting the temporalis muscle inferiorly. This muscle has a rich blood supply via the deep temporal branches of the internal maxillary artery that allows its use in reconstruction after maxillectomy or parotidectomy.

The facial nerve exits the mastoid through the stylomastoid foramen and enters the substance of the parotid gland. The carotid canal lies medial to the tip of the tympanic portion of the temporal bone. Posterolaterally lies the jugular foramen, which transports cranial nerves IX, X, and XI. The hypoglossal canal and its accompanying nerve are found posteromedial to the carotid canal.

The middle meningeal artery enters foramen spinosum just medial to the glenoid fossa. Also medial to the glenoid fossa is the petrotympanic fissure and the exiting chorda tympani. Progressing anteromedially past the foramen spinosum are the foramen ovale, the cartilaginous eustachian tube, the ICA, and the foramen lacerum. The relationship of these structures can be depicted by a series of 3 parallel lines situated at 45° to the midsagittal plane (see Image 3).

The medial and lateral pterygoid muscles take up most of the space of the infratemporal fossa. The structures of importance near these muscles are the mandibular branch of the trigeminal nerve, the pterygoid plexus of veins, and branches of the maxillary arteries. Deeper still are the cartilaginous eustachian tube and the tensor and levator veli palatini muscles.

Moving anteriorly past the pterygoid process, one finds the pterygomaxillary fissure, which transmits the maxillary artery to the pterygomaxillary fossa. The greater petrosal nerve joins the deep petrosal nerve to form the vidian nerve, which enters the fossa via the vidian or pterygoid canal en route to the pterygopalatine ganglion. The maxillary nerve enters through the foramen rotundum and branches thereafter to supply sensory information from regions of the face. Both nerves send branches to the parasympathetic sphenopalatine ganglion. The IOF is at the most anterior limit of the pterygomaxillary fossa and is continuous with the infratemporal fossa.

Medial structures

The sphenoid sinus serves as an access route to the pituitary and the clivus. Sellar pneumatization of the sinus allows easier entry during transphenoidal approaches. It is important to avoid disruption of the lateral wall during instrumentation, as the ICA and optic nerve are found just lateral to a thin margin of bone. Sometimes, a dehiscence may be present in the lateral wall exposing the vidian nerve as well.

Posterior and inferior to the sphenoid sinus along the midline lies the nasopharynx. The lateral walls are formed from mucosa, pharyngobasilar fascia, and the superior pharyngeal constrictor muscle. The sinus of Morgagni is the potential space between the muscle and the skull base and is an important area of potential spread of tumor or infection from the nasopharynx. This space is occupied by the eustachian tube and the tensor and levator veli palatini muscles. Directly superior to the nasopharynx is the foramen lacerum and the ICA, just prior to its entry into the cavernous sinus.

The investing fascia of the nasopharynx, the pharyngobasilar fascia, is suspended from the skull base and clivus located superiorly. The clivus is formed by the sphenoid and occipital bones. Posterior to the clivus lie the vertebrobasilar artery and the brainstem.

Boundaries

The anterior limit of the posterior skull base is formed by the clivus (medially), the posterior aspects of the sphenoidal body, and the basioccipital bone. The posterior limit is the occipital bone. The lateral walls are formed from the posterior surface of the petrous bone and mastoid portions of the temporal bones. The overlying tentorium cerebelli separates the cerebellum from the cerebral hemispheres above, while the lateral walls and floor are formed from the occipital bone.

The floor is grooved for the cerebellar hemispheres and the midline internal occipital crest runs from the foramen magnum to the internal occipital protuberance (IOP). The crest serves as an attachment for the falx cerebelli, which contains the occipital sinus. Grooves for the superior sagittal sinus are superior to the IOP. Lateral to the IOP are the horizontal grooves for the paired transverse sinuses, which descend to the mastoid angle of the parietal bone and become continuous with the sigmoid sulcus. The sigmoid sinuses run anteroinferiorly then inferomedially and end at the jugular foramen. The sulcus for the inferior petrosal sinus sits posterior to the clivus and anterior to the petrous apex (see Image 8).

Foramina

The porus acusticus is the opening for the IAC and sits on the posterior surface of the petrous bone. This is a pathway for the cranial nerves VII and VIII, the nervus intermedius, and branches of the anterior inferior cerebellar artery en route to the inner ear. The second foramen in this region is the vestibular aqueduct, which is posterior and inferior to the IAC. It transmits the endolymphatic duct.

Below this area lies the jugular foramen. It is formed by the anterior processus jugularis of the petrous bone and the occipital bone posteriorly, and it lies at the posterior end of the petrooccipital fissure. The sigmoid sinus and jugular bulb enter the foramen at its smooth, posterior end (pars vascularis) and cranial nerves IX, X, and XI enter its rougher, anterior end (pars nervosa). The inferior petrosal sinus usually enters this portion of the jugular foramen between cranial nerves IX and X, but its

path is highly variable; it may even enter the internal jugular vein below the skull base. Lastly, the ascending pharyngeal artery may send a posterior meningeal branch via the jugular foramen.

The hypoglossal foramen is located inferomedially and transmits the hypoglossal nerve (XII), a meningeal branch of the ascending pharyngeal artery, and the hypoglossal venous plexus. Emissary veins may leave the posterior fossa via mastoid foramina.

The brainstem communicates with the vertebral canal via the foramen magnum. The structures that pass through are the medulla oblongata, spinal accessory nerve, vertebral and posterior spinal arteries, and the apical ligament of the dens and membrane tectoria.

Contents

The midbrain, pons, medulla, and the cerebral and cerebellar hemispheres lie within the posterior fossa. The various venous sinuses mentioned earlier are enclosed by the dura mater and tentorium cerebelli. Cranial nerves VII through XII exit through the posterior fossa. Cranial nerves VII and VIII and the nervus intermedius exit through the porus acusticus, nerves IX, X, and XI traverse the jugular foramen, and XII exits via the hypoglossal canal.

Upon entering the posterior fossa via the foramen magnum, the vertebral arteries ascend ventral to the roots of cranial nerves IX, X, and XI. The posterior inferior cerebellar arteries (PICA) usually branch off from the vertebral arteries prior to forming the midline basilar artery at the base of the pons. The basilar artery then branches into the anterior inferior cerebellar arteries, which travel to the cerebellopontine angle in close relationship to cranial nerves VII and VIII. The basilar artery then branches into the labyrinthine, numerous long and short pontine arteries, and, lastly, the superior cerebellar arteries, which make up the posterior portion of the circle of Willis (see Image 9).

Inferior relationships

A surgeon must have knowledge of the outer regions of the skull base as these regions often serve as access points during surgery.

Suboccipital region

The mastoid tip serves as the origin for the sternocleidomastoid, while the posterior digastric muscle originates deep to this area. Posteriorly, the trapezius muscle is the most superficial, and immediately deeper lie the splenius capitis and cervicis muscles and the semispinalis capitis muscle. Upon reflection of these muscles from the superior nuchal line, the suboccipital triangle is exposed (see Image 10).

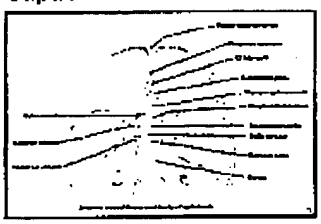
The suboccipital triangle is superficial to the ligaments connecting the atlas to the axis and contains the occipital artery, vertebral artery, a complex of veins, the greater occipital nerve, and the C-1 nerve. The occipital artery courses posteriorly deep to the mastoid tip. Surgical approaches in this area allow mobilization of the vertebral artery and access to the foramen magnum.

Vertebral artery

The vertebral artery originates from the subclavian artery and has 4 parts, the cervical, foraminal, atlantic, and subarachnoid. The atlantic portion is encountered in the suboccipital triangle of the nuchal region and is covered by the semispinalis capitis muscle.

The atlantic portion exits the atlas at the transverse foramen medial to the lateral rectus capitis muscle and curves posteriorly behind the lateral mass of the atlas. It then passes medially along the groove on the posterior arch of the atlas and pierces the atlantooccipital membrane to enter the vertebral canal and subarachnoid space. The subarachnoid portion of the artery is considered to lie in the posterior cranial fossa proper.

Caption: Picture 1. Skull base anatomy. Anterior cranial fossa.



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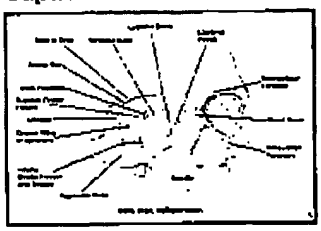
Caption: Picture 2. Skull base anatomy. Orbit anatomy.



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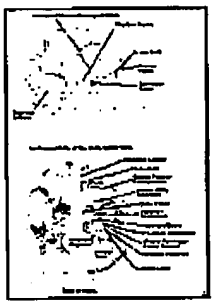
Caption: Picture 3. Skull base anatomy. Skull base foramina.



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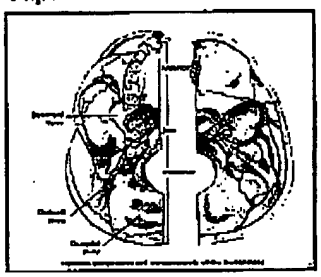
Caption: Picture 4. Skull base anatomy. Bones of the skull base.



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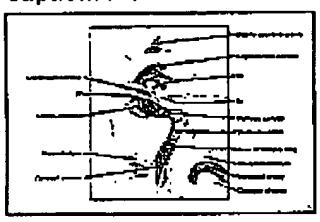
Caption: Picture 5. Skull base anatomy. Internal carotid artery intracranial course.



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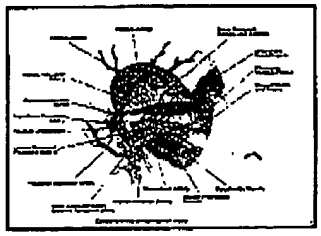
Caption: Picture 6. Skull base anatomy. Infratemporal fossa.



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Caption: Picture 7. Skull base anatomy. Oblique view of skull base.

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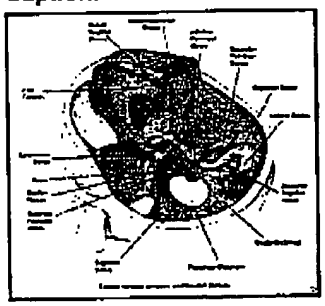
Caption: Picture 8. Skull base anatomy. Venous sinuses.



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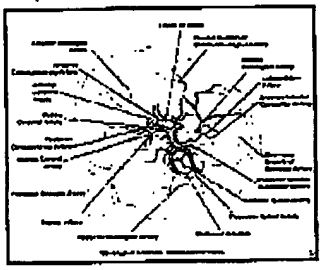
Caption: Picture 9. Skull base anatomy. Circle of Willis.



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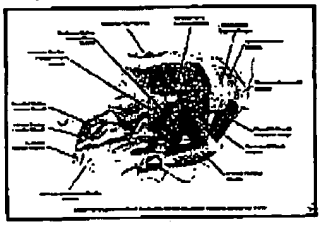
Caption: Picture 10. Skull base anatomy. Suboccipital triangle.



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